

APPENDIX
Claims as Amended

1. (Once amended) A composition for enhancing transport [or release through cell membranes, between cells, cell barriers or lipid membranes] through lipid-containing membranes comprising

[a membrane barrier transport enhancing agent selected from the group consisting of polymers changing structure or properties in response to at least one stimulus, peptides which are hydrophobic and form pores in cell membranes as a function of a change in pH, and phospholipid disrupting agents, and

means for inducing or enhancing the effectiveness of the agent to disrupt the membrane] a pH-sensitive polymer which is not hydrophobic at about pH 7.4, but which is hydrophobic and disrupts a lipid-containing membrane at a pH between about 5 and about 6.5,

a second polymeric or monomeric unit conjugated to, complexed with, or incorporated into the pH- sensitive polymer, which polymeric or monomeric unit enhances disruption of the membrane or bonds to a carrier or a therapeutic or diagnostic agent.

2-4. (Canceled).

5. (Once amended) The composition of claim 1 [for transport into or through cells, cell membranes, or a cell barrier comprising the membrane barrier transport enhancing agent in combination with] further comprising a diagnostic or therapeutic agent.

6. (Canceled).

7. (Once amended) The composition of claim [6] 1 wherein the [pH sensitive polymer is graft copolymer, block copolymer, random copolymer or blends comprising] first polymer and the second polymeric or monomeric unit form a graft copolymer, block copolymer, random copolymer or blend [monomeric units prepared from monomers selected from the group consisting of acrylic acid, C₁₋₆ straight chain, branched, and cyclic 2-alpha-alkyl acrylic acids, esters of acrylic acid copolymerized with acrylic acid, polymers including one or more polymeric blocks comprising proteins or peptides which include imidazole groups].

8. (Once amended) The composition of claim 1 wherein the [membrane barrier transport enhancing agent] second polymeric or monomeric unit is coupled with a ligand binding to the surface of a cell.

9. The composition of claim 1 further comprising a compound which decreases lysosomal degradation.

10. The composition of claim 5 wherein the therapeutic agent is a cytotoxic compound.

11. (Once amended) The composition of claim 1 [further comprising] wherein the second polymer is a polycationic polymer.

12. (Once amended) The composition of claim 5 wherein the therapeutic agent is a nucleoside, nucleotide, [nucleic acid,] or nucleic acid [molecule].

13. (Once amended) The composition of claim 1 further comprising a carrier selected from the group consisting of microparticles, nanoparticles, micelles and liposomes[, emulsion and lipid vesicles].

14. (Canceled).

15. (Once amended) A method for enhancing transport [or release through cell membranes, between cells, cell barriers or lipid membranes] of agents through lipid-containing membranes comprising administering to the [cells, cell membranes, cell layer, cell barrier, or lipid membranes any of the compositions of claims 1-14] lipid-containing membrane any of the compositions of claims 1, 5, 7-13, and 26-32.

16. (Canceled).

17. The method of claim 15 wherein the composition is administered to cells in a suspension.

18. The method of claim 15 wherein the composition is administered to layers of cells to enhance transport through the cell layers.

19. The method of claim 15 wherein the composition is administered to lipid membranes to enhance transport of molecules into or out of the lipid membranes.

20. (Once amended) The method of claim 15 wherein the composition is administered in

combination with [electrophoresis or iontophoresis] electrophoresis or iontophoresis.

21. (New) The method of claim 15 further comprising application of a stimulus means to further enhance the effectiveness of the composition to disrupt the membrane, wherein the stimulus means induces a change in the structure of the polymer of the composition.

22. (New) The method of claim 21 wherein the stimulus means is selected from the group consisting of pH, light, ionic strength, solvent composition, temperature, and electric field.

23. (New) The method of claim 15 further comprising administration of a stimulus means to further enhance the effectiveness of the composition to disrupt the membrane, wherein the stimulus means is selected from the group consisting of ultrasound, electrical fields, radiation, and combinations thereof.

24. (New) The method of claim 23 wherein the stimulus means is ultrasound.

25. (New) The method of claim 24 wherein the ultrasound is administered at between 20 kHz and 10 MHz.

26. (New) The composition of claim 11 wherein the polycationic material is selected from the group consisting of chitosan, polylysine, polyethyleneimine, and N,N-dimethylaminoethyl methylacrylate.

27. (New) The composition of claim 13 wherein the carrier is a micelle or liposome.

28. (New) The composition of claim 7 wherein the second polymeric or monomeric unit is selected from the group consisting of acrylic acid; C₁₋₆ straight chain, branched, and cyclic 2-alpha-alkyl acrylic acids; and esters of acrylic acid copolymerized with acrylic acid.

29. (New) The composition of claim 7 wherein the second polymeric or monomeric unit are polymeric blocks comprising proteins or peptides which include imidazole groups.

30. (New) The composition of claim 1 wherein the second polymeric or monomeric unit is a lipid or phospholipid.

31. (New) The composition of claim 1 wherein the second polymeric or monomeric units comprise sulfonated groups.

32. (New) The composition of claim 1 wherein the second polymeric or monomeric unit

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is sensitive to a stimulus selected from the group consisting of temperature, light, electrical stimuli, radiation, and ion concentration.